SYNTHETIC COMPLEMENTARY PEPTIDES AND OPHTHALMOLOGIC USES THEREOF

BACKGROUND OF THE INVENTION

Cross-reference to Related Application

This patent application claims benefit of provisional patent application U.S. Serial number 60/123,409, filed March 9, 1999.

Federal Funding Legend

This invention was produced in part using funds obtained through a grant from the National Institutes of Health (MH52527) and National Eye Institute EY04716. Consequently, the federal government has certain rights in this invention.

Field of the Invention

The present invention relates generally to the biochemical pharmacology of ophthalmologic agents. More

specifically, the present invention relates to synthetic complementary peptides and ophthalmologic uses thereof.

Description of the Related Art

Alkali-injury of the eye provokes an acute inflammatory reaction, largely composed of polymorphonuclear leukocytes (PMNs), which are responsible for corneal ulcerations and perforations.[1-3] N-acetyl-PGP and N-methyl-PGP, neutrophilic chemoattractants released during direct alkaline hydrolysis of corneal proteins, are the initial triggers for polymorphonuclear leukocyte invasion into the alkali-injured cornea.[4-6] The specific activity of N-acetyl-PGP is greater than the methylated tripeptide.[4]

Recognition that N-acetyl-PGP is an important mediator in this disease has opened a therapeutic window of opportunity. Early inhibition of this chemoattractant in an alkali-injured eye might reduce or eliminate the first neutrophilic influx. Minimizing the number of neutrophils initially penetrating into the damaged cornea would limit the production of secondary inflammatory mediators, such as leukotriene B_4, hence reducing the additional

recruitment of polymorphonuclear leukocytes. Exclusion of neutrophils from the alkali-injured cornea is the key to decreasing or eliminating corneal ulceration. It is therefore of paramount importance to search for lead compounds which can inhibit this chemoattractant.

One approach to the development of a lead inhibitory compound can be found in the molecular recognition theory.[7] This concept posits that a fundamental requirement for biological reactions is that proteinaceous molecules recognize one another in a genetically defined manner. Blalock and Smith[8] proposed a novel approach to molecular recognition which has succeeded in predicting the interactions of proteinaceous molecules with high frequency. This method, based on the development of complementary peptides specified by ligand antisense RNA, has proven useful in designing interactive peptides, isolating receptors, and producing anti-receptor and anti-idiotypic antibodies.[9,10]

Thus, the prior art is deficient in synthetic complementary peptides to treat ophthalmologic disorders. The